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**GROUP 1600**  
**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**  
**BOARD OF PATENT APPEALS AND INTERFERENCES**

APPLICANT: William McBride, et al.  
 SERIAL NO.: 08/253,973 EXAMINER: M. Hartley  
 FILING DATE: June 3, 1994 GROUP: 1616  
 TITLE: MONOAMINE, DIAMIDE, THIOL-CONTAINING METAL  
 CHELATING AGENTS

*P. TUCK*  
*#41*  
*12/17/99*

Assistant Commissioner for Patents  
 Washington, D.C. 20231

**CERTIFICATE OF FACSIMILE TRANSMISSION PURSUANT TO  
 37 CFR 1.8**

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 below.

*Patricia A. McDaniels*  
 Patricia A. McDaniels

Date: December 7, 1999

Sir:

**REPLY BRIEF**

This Brief is submitted in response to the Examiner's Answer dated October 13, 1999. Authorization is hereby given to charge the fee of \$150.00, and any other fee which may be due with regard to this submission, or to credit any overpayment, to Deposit Account No. 50-0452.

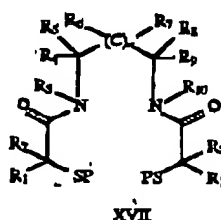
**I. The Examiner has materially misrepresented the disclosure of Harris.**

At pages 5 and 6, the Examiner's Answer states that:

Harris discloses that the "preferred" compounds are a "diaminedithiol" (e.g., see column 4, line 59-60), however, the formula which is disclosed by Harris clearly encompasses monoamine, diamide, single thiol ligands which are similar to those instantly claimed (e.g., only excluding a targeting moiety).

... Harris specifically disclosed compounds which are not "diaminethiols" and are encompassed by the disclosed formula. For example, compounds XVII (column 8) XIX (column 9) are specifically disclosed species' [sic] which are not diaminethiols, but which are encompassed by the formula shown in column 3. Since Harris discloses a general formula with specific substitutions, the entire genus of the formula is taught by Harris. Further more, the express statement of Harris of "diaminethiol" appears to describe the general formula having at least two nitrogen atoms and one sulfur, SNN(S or N) ligands shown by the formula in column 3.

Compound XVII is reproduced below.



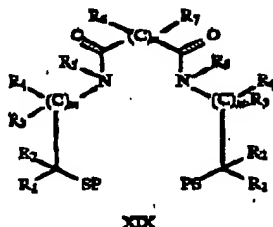
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It is clear that Formula XVII of Harris is a diamidodithiol and is thus outside the scope of the present claims.

Formula XIX of Harris is reproduced below.



It is clear that Formula XIX of Harris is a diamidodithiol and is thus outside the scope of the present claims.

Neither of Harris formulae XVII or XIX is relevant to the **monoamine, diamide, single thiol** chelator of the present claims. The Examiner's citation of formulae VVII and XIX in relation to the presently claimed formula is factually incorrect and misleading.

**II. The substitutions proposed by the Examiner would not have been made by a chemist of ordinary skill.**

At page 6 of the Answer, the Examiner states that:

... the general formula disclosed by Harris may be substituted to yield ligands which are monoamine, diamide, single thiol-containing ligands, which are within the scope of the claimed chelator.

At page 7, the position is reiterated: "... the formula disclosed by Harris clearly encompasses chelators which are monoamide [*sic*], diamide, thiols." At page 9, the Examiner again opines that the monoamine, diamide thiol chelators of the instant claims "are encompassed and taught by the formula disclosed by Harris."

The substitutions proposed by the Examiner would only occur if one of skill selectively ignored the teachings of the Harris disclosure. The Examiner has provided no evidence that one of skill actually would ignore the consistent limitations of Harris to "diaminethiols", "diaminedithiols", and "diamidodithiols". The Examiner has done no more than speculate that those of skill would have viewed the Harris formula in a vacuum, without reading or applying the limitations consistently repeated throughout the text. The

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Examiner's speculation is legally insufficient to support the present combination, as a matter of law. *In re Jones*, 21 U.S.P.Q.2d 1941, 1944 (Fed.Cir. 1992).

**III. The Harris disclosure is too vague and indefinite to place those of ordinary skill in possession of the chelator of the present claims.**

At page 7 of the Answer, the Examiner opines that:

... if the recitation of "diaminethiol" in describing the general formula in column 3 is expressly limiting, it would not be possible for Harris to disclose "diamidedithiols" which are set forth in examples. Thus the teaching of Harris is only limited to the compounds encompassed by the formula set forth in column 3.

Notwithstanding the tortuous logic of the Examiner's conclusion, the Harris language is ambiguous. It is elementary chemistry that an amine is not the same as an amide, and those of skill do not ordinarily equate the two chemical entities. The Harris disclosure contains no teaching that explains the presence of the diamidodithiol ligands and their synthesis that appears at columns 8 and 9. Indeed, the examples appearing at columns 12 through 18 disclose only biscysteine compounds, which are diaminedithiols, and the Harris claims are limited to the biscysteine compounds.

Thus Harris presents those of skill with a generic formula which only vaguely corresponds to the actual teachings of the reference. In light of such confusing ambiguity, the formula appearing at column 3 can only reasonably be construed narrowly, in light of the compounds specifically exemplified. Harris does not place those of skill in possession of the chelator of the present claims.

**IV. No *prima facie* case of obviousness has been established.**

Appellants have identified specific reasons to rebut any inference of motivation to combine Harris and Fritzberg to obtain the present invention:

- different organs are targeted by the references
- the combination would have been inoperable
- the combination does not yield the present invention

The Examiner has failed to identify a single piece of evidence to support his conclusion that merely because Harris and Fritzberg are both in the field of

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radiopharmaceuticals, those of skill would have been motivated to combine the references. The Examiner's conclusion is based on mere speculation, and is insufficient as a matter of law. In fact, the statement that Appellants' evidence of inoperability of the combination

... is not found persuasive because Fritzberg teaches that various targeting moieties may be used and conjugated to ligands. The targeting moieties bind to various desired sites, such as cancer cells, etc. (see columns 8-9) and would therefore be expected to provide the advantage of site-specificity to various desired sites. . .

appears to completely ignore rebuttal evidence, in contravention of black letter law. *See, In re Piaseki*, 223 U.S.P.Q. 785, 787-788 (Fed.Cir. 1984).

The statement at pages 8 and 9 of the Answer similarly ignores the requirements of settled law:

... Fritzberg is not being used to modify the basic formula of Harris to arrive at monoamine, diamine [*sic*] thiol chelators as instantly claimed. As set forth, such ligands are encompassed and taught by the formula disclosed by Harris. Fritzberg is being used to show that it is known in the art that such radiopharmaceutical ligands may be conjugated to such radiopharmaceutical chelators as [*sic*] various positions, via various linkers to provide the advantage of site specificity.

The Court has stated that "... generalization should be avoided insofar as specific chemical structures are alleged to be *prima facie* obvious one from the other." *In re Grabiak*, 226 U.S.P.Q. 870, 872 (Fed.Cir. 1985). The Court has also emphasized that

[t]he mere fact that it is *possible* to find two isolated disclosures which might be combined in such a way to produce a new compound does not necessarily render such production obvious unless the art also contains something to suggest the desirability of the proposed combination. (*emphasis in original*).

*Id.*, citing *In re Bergel*, 130 U.S.P.Q. 206, 208 (C.C.P.A. 1961). The Examiner cannot rely on a generalized belief that references may be combined in the absence of a specific suggestion in the references to support the combination.

Finally, the Examiner's reliance on *In re McLaughlin*, 170 U.S.P.Q. 209 (C.C.P.A. 1971) is misplaced. *In re Oetiker*, 24 U.S.P.Q.2d 1443, 1445 (Fed.Cir. 1992), cited by the Examiner, does not stand for the proposition that merely because two references are in the same field of endeavor, they may be combined without a teaching or suggestion to support the combination. The portion of *In re Oetiker* cited by the Examiner addressed a combination of a reference relating to a hose clamp fastening (or "hook") with a reference relating to a hook and eye fastener for garments. *Id.* In fact, the combination suggested by the PTO in *In re Oetiker* was overruled. *Id.* at 1446.

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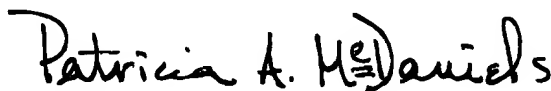
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In conclusion, Appellants request that the rejection of claims 2-8 and 10 of the present application be overruled, that the claims be found to be allowable, and that Appellants' Request for Interference pursuant to 37 C.F.R. 1.607(b) be expeditiously acted upon.

Respectfully submitted,

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